

WHAT IS CLAIMED IS:

1. An oral dosage form, comprising
an orally therapeutically effective amount of an opioid agonist, and
an opioid antagonist, the ratio of opioid antagonist to opioid agonist providing a
combination product which is analgesically effective when the combination is administered
orally, but which is aversive in physically dependent human subjects when administered at the
same dose or at a higher dose than the usually prescribed dose of the opioid agonist.
2. The oral dosage form of claim 1, wherein the amount of antagonist included in the
oral dosage form causes an aversive experience in a physically dependent addict taking about 2-3
times the usually prescribed dose of the opioid.
3. The oral dosage form of claim 1, wherein the opioid agonist is hydrocodone and
the antagonist is naltrexone.
4. The oral dosage form of claim 3, wherein the ratio of naltrexone to hydrocodone
is from about 0.03:1 to about 0.27:1.
5. The oral dosage form of claim 3, wherein the ratio of naltrexone to hydrocodone
is from about 0.05:1 to about 0.20:1.
6. The oral dosage form of claim 1, wherein the opioid agonist or analgesic is
selected from the group consisting of morphine, hydromorphone, hydrocodone, oxycodone,
codeine, levorphanol, meperidine, methadone, and mixtures thereof.
7. The oral dosage form of claim 1, further comprising an additional non-opioid drug
selected from the group consisting of an NSAID, a COX-2 inhibitor, acetaminophen, aspirin, an
NMDA receptor antagonist, a drug that blocks a major intracellular consequence of NMDA-

receptor activation, an antitussive, an expectorant, a decongestant, an antihistamine and mixtures thereof.

8. The oral dosage form of claim 1, further comprising one or more pharmaceutically acceptable inert excipients.

9. The oral dosage form of claim 6, wherein said opioid antagonist is selected from the group consisting of naltrexone, naloxone, nalmephen, cyclazocine, levallorphan, and mixtures thereof.

10. The oral dosage form of claim 6, wherein said opioid antagonist is naltrexone.

11. The oral dosage form of claim 1, further comprising a sustained release carrier which imparts sustained release properties to said opioid agonist.

12. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is oxycodone, wherein the ratio of naltrexone to oxycodone is from about 0.037:1 to about 0.296:1.

13. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is codeine, wherein the ratio of naltrexone to codeine is from about 0.005:1 to about 0.044:1.

14. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is hydromorphone, wherein the ratio of naltrexone to hydromorphone is from about 0.148:1 to about 1.185:1.

15. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is levorphanol, wherein the ratio of naltrexone to levorphanol is from about

0.278:1 to about 2.222:1.

16. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is meperidine, wherein the ratio of naltrexone to meperidine is from about 0.0037:1 to about 0.0296:1.

17. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is methadone, wherein the ratio of naltrexone to methadone is from about 0.056:1 to about 0.444:1.

18. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is morphine, wherein the ratio of naltrexone to morphine is from about 0.018:1 to about 0.148:1.

19. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is oxycodone, wherein the ratio of naltrexone to oxycodone is from about 0.056:1 to about 0.222:1.

20. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is codeine, wherein the ratio of naltrexone to codeine is from about 0.0083:1 to about 0.033:1.

21. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is hydromorphone, wherein the ratio of naltrexone to hydromorphone is from about 0.222:1 to about 0.889:1.

22. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is levorphanol, wherein the ratio of naltrexone to levorphanol is from about 0.417:1 to about 1.667:1.

23. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is meperidine, wherein the ratio of naltrexone to meperidine is from about 0.0056:1 to about 0.022:1.

24. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is methadone, wherein the ratio of naltrexone to methadone is from about 0.083:1 to about 0.333:1.

25. The oral dosage form of claim 1, wherein said opioid antagonist is naltrexone and said opioid agonist is morphine, wherein the ratio of naltrexone to morphine is from about 0.028:1 to about 0.111:1.

26. A method of preventing oral abuse of an oral opioid formulation, comprising preparing an oral dosage form which comprises an orally analgesically effective amount of an opioid agonist and incorporating therein an opioid antagonist in a ratio to said opioid agonist such that the oral dosage form is analgesically effective when administered orally, but is aversive in physically dependent human subjects when administered at the same dose or at a higher dose than the usually prescribed dose of the opioid agonist.

27. The method of claim 26, wherein the amount of antagonist included in the oral dosage form causes an aversive experience in physically dependent addicts taking about 2-3 times the usually prescribed dose of the opioid.

28. The method of claim 26, wherein the opioid agonist is hydrocodone and the antagonist is naltrexone.

29. The method of claim 26, wherein the ratio of naltrexone to hydrocodone is from about 0.03:1 to about 0.27:1.

30. The method of claim 26, wherein the ratio of naltrexone to hydrocodone is from about 0.05:1 to about 0.20:1.

31. The method of claim 26, herein the opioid agonist or analgesic is selected from the group consisting of morphine, hydromorphone, hydrocodone, oxycodone, codeine, levorphanol, meperidine, methadone, and mixtures thereof and the opioid antagonist is selected from the group consisting of naltrexone, naloxone, nalmephe, cyclazocine, levallorphan, and mixtures thereof.

32. The method of claim 26, wherein the opioid antagonist is naltrexone and the opioid agonist is selected from the group consisting of hydrocodone in a naltrexone:hydrocodone ratio from about 0.03:1 to about 0.27:1; oxycodone in a naltrexone/oxycodone ratio from about 0.037:1 to about 0.296:1; codeine in a naltrexone/codeine ratio from about 0.005:1 to about 0.044:1; hydromorphone in a naltrexone/ hydromorphone ratio from about 0.148:1 to about 1.185:1; levorphanol in a naltrexone/levorphanol ratio from about 0.278:1 to about 2.222:1; meperidine in a naltrexone/meperidine ratio from about 0.0037:1 to about 0.0296:1; methadone in a naltrexone/methadone ratio from about 0.056:1 to about 0.444:1; and morphine in a naltrexone/ morphine ratio from about 0.018:1 to about 0.148:1.

33. The method of claim 26, wherein the opioid antagonist is naltrexone and the opioid agonist is selected from the group consisting of hydrocodone in a naltrexone:hydrocodone ratio from about 0.05:1 to about 0.20:1; oxycodone in a naltrexone/oxycodone ratio from about 0.056:1 to about 0.222:1; codeine in a naltrexone/codeine ratio from about 0.0083:1 to about 0.033:1; hydromorphone in a naltrexone/ hydromorphone ratio from about 0.222:1 to about 0.889:1; levorphanol in a naltrexone/levorphanol ratio from about 0.417:1 to about 1.667:1; meperidine in a naltrexone/meperidine ratio from about .0056:1 to about 0.022:1; methadone in a naltrexone/methadone ratio from about 0.083:1 to about 0.333:1; and morphine in a naltrexone/ morphine ratio from about 0.028:1 to about 0.111:1.

34. The method of claim 32, further comprising incorporating into said oral dosage form an additional non-opioid drug selected from the group consisting of an NSAID, a COX-2 inhibitor, acetaminophen, aspirin, an NMDA receptor antagonist, a drug that blocks a major intracellular consequence of NMDA-receptor activation, an antitussive, an expectorant, a decongestant, an antihistamine and mixtures thereof.

35. The method of claim 26, further comprising preparing said oral dosage form with a sustained release carrier such that the dosage form is administrable on a twice-a-day or on a once-a-day basis.